REMARKS/ARGUMENTS

Claims 1-14 are pending.

Citations to the Specification are directed to U.S. Patent Application Publication No. 2005/0154052 (Parthasaradhi et al.)

Favorable reconsideration is respectfully requested in view of the foregoing amendments and the following remarks.

Rejection under 35 USC 102(b)

Claims 1-2 stand rejected under 35 USC 102(b) over U.S. Patent No. 4,943,590 (Boegesoe et al.). This rejection is respectfully traversed.

The Examiner argues that the instant claims and the prior art disclosure is different in the measurements of crystallinity by powdered X-ray diffraction, and notes that the innate nature of a product, such as the X-ray diffraction pattern does not demarcate from a product which although was not measured by X-ray but are made by the same identical process of crystallization from acetone as the original claims and the specification. The Examiner further argues that no factual evidence was provided by applicants that the instant example 1 and example 2 are different in crystal form.

However, while the '590 patent discloses crystallization from acetone (see e.g. Example 2), the instant application discloses that (S)-citalopram oxalate is mixed with acetone, heated to reflux and cooled to 20°C, then the separated crystals are filtered (see ¶[0017] Example 1). As set forth in the Response filed February 12, 2009, the Banga reference teaches that different crystalline modifications arise under varied experimental conditions, including, inter alia, thermal treatment. Thus given the varying conditions used for making the claimed Form I (S)-citalopram oxalate, the art teaches that the claimed polymorph will be expected to have a different crystalline form from that produced in the '590 patent. As shown in the Banga reference, the assumption that crystallization using distinct thermal profiles and solvents will produce the same polymorph has no basis in fact.

Accordingly, the art teaches that XRPD data is reliable to differentiate between different polymorphic crystalline forms. Applicant has provided XRPD data for the claimed polymorphic form of citalopram oxalate, and demonstrated that the form as taught in the '590 patent is distinct from the claimed polymorphic form.

Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

Rejections under 35 USC 112 first paragraph

Claims 1-2 stand rejected under 35 USC 112 first paragraph as allegedly failing to comply with the written description requirement. This rejection is respectfully traversed.

Claim 1-2 and 3-7 stand rejected under 35 USC 112 first paragraph as allegedly lacking enablement. This rejection is respectfully traversed.

The Examiner sets forth that if the product made by using ethylacetate, methyl tert-butyl ether and acetonitrile is different from the product made using acetone as exemplified in examples 1, 2 or 5, then, such product must be supported by side-by-side comparison with the prior art product made by acetone. The Examiner further sets forth that, the product being claimed by the process with acetone and without acetone as amended, was declared by oath to be "identical", and that every exemplification wherein form I was obtained employed acetone (see examples 1, 2, 5). The Examiner argues that no where in the specification provided description or enablement as to what is the product being made by using ethylacetate, methyl tert-butyl ether and acetonitrile.

The Examiner sets forth that the Specification provided no description or enablement that the instantly amended process would produce form I as described by examples 1, 2 or 5 which used exclusively acetone. Therefore, claims 1-2 would be considered to contain new matter since a product which is different from those made in acetone was not disclosed.

However, to satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. See, e.g., *Moba, B.V. v. Diamond Automation, Inc.*, 325 F.3d 1306, 1319, 66 USPQ2d 1429, 1438 (Fed. Cir. 2003); *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d at 1563, 19 USPQ2d at 1116. An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997). Possession may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was "ready for patenting" such as by the disclosure of drawings or structural chemical formulas that show that the invention was

complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention. See, e.g., *Pfaff v. Wells Elecs., Inc.*, 525 U.S. 55, 68, 119 S.Ct. 304, 312, 48 USPQ2d 1641, 1647 (1998); Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406; *Amgen, Inc. v. Chugai Pharmaceutical*, 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991) (one must define a compound by "whatever characteristics sufficiently distinguish it").

Here, the written description requirement is met because the Specification includes working examples which show a process of making Form I (S)-citalopram using ethyl acetate, methyl tert-butyl ether, dioxane and acetonitrile (see ¶[0008] and ¶[0009]).

The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation. United States v. Telectronics, Inc., 857 F.2d 778, 785 (Fed. Cir. 1988). A specification disclosure which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as being in compliance with the enablement requirement of 35 USC 112, first paragraph, unless there is a reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support. Assuming that sufficient reason for such doubt exists, a rejection for failure to teach how to make and/or use will be proper on that basis. In re Marzocchi, 439 F.2d 220, 224 (CCPA 1971). Here, the claims are enabled because there is not any reason to doubt the objective truth of the statements contained in the Specification for enabling support. The Specification discloses the manner and process for making and using the claimed invention, including working examples which show the efficacy of the claimed invention (see ¶[0017], ¶[0018]). For example, the Specification discloses a process of making Form I (S)-citalopram using ethyl acetate, methyl tert-butyl ether, dioxane and acetonitrile (see ¶[0008] and ¶[0009]).

Thus, given the teachings of the Specification, the quantity of experimentation required is not excessive in view of the subject matter of the claims. The Specification sets forth several methods for producing a (S)-citalopram, and the two novel crystalline forms of (S)-citalopram. Working Examples are also provided, as well as detailed information as to the methods. This information can be used by one of ordinary skill in the art to determine appropriate conditions to

practice the claimed process, without undue experimentation.

Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

Rejection under 35 USC 102(e)

Claims 8-9 and 16 stand rejected under 35 USC 102(e) as being anticipated by U.S. Patent No. 6,916,941 (Christensen et al.). This rejection is respectfully traversed.

The Examiner argues that a product cannot be separated from its innate nature such as the physical properties of the product i.e. x-ray diffraction pattern, and notes that the product as claimed which was described by the specification to be made by any alcoholic solvent, and that, the mere deletion of ethanol from the process of making does not obviate the anticipation. If the product which is made by methanol or isopropyl alcohol is a different product from the one made by ethanol, only a side-by-side comparison of the instant product with the prior art product can support such an allegation.

However, the claims are directed to crystalline Form II of (S)-citalopram oxalate, with the claimed XRPD data. While the '941 Christensen patent discloses a method for the manufacture of crystalline particles of (S)-citalopram oxalate by crystallization from ethanol, this is different form the claimed method. In the method of synthesis of Form II (S)-citalopram oxalate of the instant claims is not dissolved from ethanol or acetone, but from methanol or isopropyl alcohol. In addition, in the method as disclosed in the '941 patent, it was necessary to seed the ethanolic solvent with escitalopram oxalate. This is in contrast to the method as disclosed in the instant application (see Examples 3, 4, and 6), which do not require a seeding step. As set forth above, the Banga reference teaches that different crystalline modifications arise under varied experimental conditions, including, inter alia, thermal treatment. Thus given the varying conditions used for making the claimed Form II (S)-citalopram oxalate, the claimed polymorph will be expected to have different crystalline form from that produced in the '941 patent

With regard to the new matter rejection, as set forth above, the Specification exemplifies the preparation of the claimed form II (S)-citalopram oxalate, therefore no new matter has been added.

Accordingly, reconsideration and withdrawal of the rejections is respectfully requested.

Rejections under 35 USC 112 first paragraph

Claims 8-9 stand rejected under 35 USC 112 first paragraph as failing to comply with the written description requirement. This rejection is respectfully traversed.

Claims 10-11, 13-14 stand rejected under 35 USC 112 first paragraph as failing to comply with the enablement requirement. This rejection is respectfully traversed.

The Examiner sets forth that no where in the specification have provided evidence that methanol alone without anti-solvent diisopropyl ether will give the form II, and argues that the exclusive disclosure of methanol/di-isopropylether and isopropanol in a field of extreme high degree of experimentation is tantamount to a teaching way from using any other solvent absent of factual support.

However, the claims are enabled because there is not any reason to doubt the objective truth of the statements contained in the Specification for enabling support. The claims are directed to a crystalline Form II (S)-citalopram oxalate, and a process of making crystalline Form II (S)-citalopram oxalate. The Specification discloses the manner and process for making and using the claimed invention, including working examples which show the efficacy of the claimed invention. For example, the instant application discloses several methods for preparing (see Examples 3, 4, and 6) form II (S)-citalopram oxalate, and the Specification discloses a process of making Form II (S)-citalopram using ethyl acetate, methyl tert-butyl ether, dioxane and acetonitrile (see ¶[0009] and ¶[0010]).

Thus, given the teachings of the Specification, the quantity of experimentation required is not excessive in view of the subject matter of the claims. The Specification sets forth several methods for producing a (S)-citalopram, and the two novel crystalline forms of (S)-citalopram. Working Examples are also provided, as well as detailed information as to the methods. This information can be used by one of ordinary skill in the art to determine appropriate solution conditions to practice the claimed process, without undue experimentation.

Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

Rejection under 35 USC 112 first paragraph

Claims 1-14 stand rejected under 35 USC 112 first paragraph as failing to comply with the written description requirement. This rejection is respectfully traversed.

The requirements for complying with the written description requirement have been set

forth above. Here, the written description requirement is met because the Specification includes working examples which show a process of making Form I (S)-citalopram using ethyl acetate, methyl tert-butyl ether, dioxane and acetonitrile (see ¶[0008] and ¶[0009]). In addition, the instant Specification discloses several methods for preparing (see Examples 3, 4, and 6) form II (S)-citalopram oxalate, and the Specification discloses a process of making Form II (S)-citalopram using ethyl acetate, methyl tert-butyl ether, dioxane and acetonitrile (see ¶[0009] and ¶[0010]).

Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

Rejection under 35 USC 103(a)

Claims 1-7 stand rejected under 35 USC 103(a) over US 4,943,590 (Boegesoe) in view of Cheronis supplemented with US 6,960,613 (Sanchez et al.), US 6,768,011 (Rock et al.) or US 7,112,686 (Humble et al.) and claims 8-14 stand rejected under 35 USC 103(a) over US 6,916,914 (Christensen et al.) in view of Cheronis supplemented with US 6,960,613 (Sanchez et al.), US 6,768,011 (Rock et al.) or US 7,112,686 (Humble et al.). This rejection is respectfully traversed.

The Examiner sets forth that Applicants' argument is that each reference differed from the claims and there is no reasonable expectation of success when prior art processes were modified, but argues that the all references recited in the rejection are analogous art. The Examiner argues that one skilled in the art is deemed to be aware of all the alternative choices of solvents for crystallization of (S)-citalopram oxalate. The Examiner argues that the motivation of obtaining purer, better crystals would have suggested to one skilled in the art to employ those alternative choices of solvents explicitly disclosed by Sanches, Rock or Humbel during crystallization of citalopram oxalate with the expectation that crystalline forms would be resulted. Such prima facie obviousness cannot be negated just because one gives the crystalline product obtained from alternative solvents a different name, a measurement of its physical properties

The Examiner further argues that the prior art both disclosed products made by anticipatory processes and how modification of such processes can be design choices to one having ordinary skill. Applicants' allegation that the products are not the same must be supported by factual evidence in a side-by side comparison using the process including all the limitation of the instant claims and using alternative process such as the instant example 1 produced a

different product from example 2; and the instant example 3 produced a different product from example 4.

However, the claims are patentable over the combination of '590 Boegesoe or '914 Christensen in view of Cheronis supplemented with '613 Sanches, '011 Rock or '686 Humble for the following reasons. To establish a prima facie case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure. In re Vaeck, 947 F.2d 488 (Fed. Cir. 1991). MPEP 2143. To establish prima facie obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. In re Royka, 490 F.2d 981 (CCPA 1974). "All words in a claim must be considered in judging the patentability of that claim against the prior art." In re Wilson, 424 F.2d 1382, 1385 (CCPA 1970). MPEP 2143.03. It is important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does. (KSR v Teleflex, 12 S.Ct. 1727, 1740 (US 2007)).

Here, not every element of the claims is taught or suggested in the combination of '590 Boegesoe or '914 Christensen in view of Cheronis supplemented with '613 Sanches, '011 Rock or '686 Humble. The instant claims are directed to two novel polymorphs of (S)-citalopram oxalate, and methods of making them. However, the prior art relied upon by the Examiner does not teach or suggest the specific polymorphs as claimed by Applicant. The Examiner failed to demonstrate that the prior art even recognized that the claimed compound exists in different polymorphic forms, or that there is a known or obvious way to manufacture the specific polymorphic forms claimed.

The claims are directed to a crystalline Form I (S)-citalopram oxalate, and a process of making crystalline Form I (S)-citalopram oxalate, as well as being directed to a crystalline Form II (S)-citalopram oxalate, and a process of making crystalline Form II (S)-citalopram oxalate.

As set forth above, the Banga reference teaches that different crystalline modifications arise under varied experimental conditions, including, inter alia, thermal treatment. Thus given the varying conditions used for making the claimed Form I and/or Form II (S)-citalopram oxalate, the claimed polymorphs will be expected to have different crystalline form from that produced in the combination of '590 Boegesoe or '914 Christensen in view of Cheronis supplemented with '613 Sanches, '011 Rock or '686 Humble.

In addition, there is no motivation for one of skill in the art to alter the methods of the combination of '590 Boegesoe or '914 Christensen in view of Cheronis supplemented with '613 Sanches, '011 Rock or '686 Humble to arrive at the claimed method, and no reasonable expectation of success. The Examiner argues that one having ordinary skill in the art is well aware of all the pertinent art in the field.

However, the '590 Boegesoe patent does not disclose or suggest methods of preparation of (S)-citalopram oxalate crystalline forms wherein the solvent is ethyl acetate, methyl tert-butyl ether, acetonitrile, methanol or isopropyl alcohol. Since the reference does not disclose or suggest this, there is no motivation to employ the process taught by the '590 Boegesoe patent to crystallize (S)-citalopram oxalate and expect to obtain the desired product to reach the limitations of the claims, with the claimed polymorphic form, and no expectation of success.

While the '590 Boegesoe patent discloses crystallization form acetone (see e.g. Example 2), the instant application discloses that (S)-citalopram oxalate is mixed with acetone, heated to reflux and is cooled to 20°C, then the separated crystals are filtered (see Example 1). As set forth above, the Banga reference teaches that different crystalline modifications arise under varied experimental conditions, including, *inter alia*, thermal treatment.

The deficiencies of the '590 Boegesoe patent are not cured by the addition of the Cheronis supplemented with '613 Sanches, '011 Rock or '686 Humble references. None of the Cheronis, '613 Sanches, '011 Rock or '686 Humble references teaches or suggests the solvent and/or thermal profiles as set forth in the instant application and claims.

While the '941 Christensen patent discloses a method for the manufacture of crystalline particles of (S)-citalopram oxalate by crystallization from ethanol, in the method of synthesis of Form II (S)-citalopram oxalate of the instant claims is not dissolved from ethanol or acetone, but from methanol or isopropyl alcohol. In addition, in the method as disclosed in the '941 patent, it

was necessary to seed the ethanolic solvent with escitalopram oxalate. This is in contrast to the method as disclosed in the instant application (see Examples 3, 4, and 6), which do not require a seeding step.

The deficiencies of the '941 Christensen patent are not cured by the addition of the Cheronis supplemented with '613 Sanchez, '011 Rock or '686 Humble references. None of the Cheronis, '613 Sanches, '011 Rock or '686 Humble references teaches or suggests the solvent and/or thermal profiles as set forth in the instant application and claims.

Accordingly, reconsideration and withdrawal of the rejection under 35 USC 103(a) is respectfully requested.

* * *

For at least the reasons set forth above, it is respectfully submitted that the above-identified application is in condition for allowance. Favorable reconsideration and prompt allowance of the claims are respectfully requested.

Should the Examiner believe that anything further is desirable in order to place the application in even better condition for allowance, the Examiner is invited to contact Applicants' undersigned attorney at the telephone number listed below.

Respectfully submitted,

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Please charge or credit our Account No. 03-0075 as necessary to effect entry and/or ensure consideration of this submission.